

Loss of survivin in the prostate epithelium impedes carcinogenesis in a mouse model of prostate adenocarcinoma.

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Public Summary:

The inhibitor of apoptosis protein survivin is expressed in most cancers. Using the conditional PTEN deletion mouse model, we previously reported that survivin levels increase with prostate tumor growth. Here we evaluated the functional role of survivin in prostate tumor growth. First, we demonstrated that mice lacking the survivin gene in prostate epithelium were fertile and had normal prostate growth and development. We then serially, from about 10-56 weeks of age, evaluated histopathologic changes in the prostate of mice with PTEN deletion combined with survivin mono- or bi-allelic gene deletion. While within this time period most of the animals with wild-type or monoallelic survivin deletion developed adenocarcinomas, the most severe lesions in the biallelic survivin deleted mice were high-grade prostatic intra-epithelial neoplasia with distinct histopathology. Many atypical cells contained large hypertrophic cytoplasm and desmoplastic reaction in the prostatic intra-epithelial neoplasia lesions of this group was minimal until the late ages. A reduced proliferation index as well as apoptotic and senescent cells were detected in the lesions of mice with compound PTEN/survivin deficiency throughout the time points examined. Survivin deletion was also associated with reduced tumor expression of another inhibitor of apoptosis member, the X-linked inhibitor of apoptosis. Our findings suggest that survivin participates in the progression of prostatic intraepithelial neoplasia to adenocarcinoma, and that survivin interference at the prostatic intraepithelial neoplasia stages may be a potential therapeutic strategy to halt or delay further progression.

Scientific Abstract:

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